THE URINARY ELIMINATION OF BORIC ACID

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In the use of "Metheneamine" ("Hexamethylenetetramine," "Urotropine") as a urinary antiseptic, some acid is customarily administered to maintain the acidity of the urine. Boric may be and is frequently used for this purpose. However, boric acid and borates are not without physiological effect when administered in sufficiently large amounts and if elimination does not proceed promptly, and accumulation takes place because of the slowness of elimination, toxic effects may result. Instances of harm arising from boric acid and borates are recorded in the literature (1). Schattenfroh states (2): "Undoubtedly the use of boric acid and borates is fraught with danger." Their use as preservatives in foods and food products is forbidden because of the belief that their presence in the foods that are consumed would be prejudicial to health.

Voicu (3) has shown that the toxicity of boric acid to organisms that produce ammonia from urea is lowered one-third by the presence of a two per cent glucose solution. The presence of glucose in the blood stream can conceivably decrease the toxicity of borates and boric acid in the body. The glucose may react with boric acid in the same manner as does the mannitol that is used in the titration method for its quantitative estimation.

With these facts in mind the authors have undertaken to study the rate of elimination of boric acid through the urinary tract.

METHODS

The titration method is the most convenient means for the quantitative determination of boric acid, and is sufficiently reliable for use when certain precautions are observed. These precautions consist in the main in the treatment of the boron containing sample with a mineral acid to a definite acidity, titration with a standard alkali solution to a known pH in the presence of an indicator, the addition of a weighed amount of mannitol and titration to a definite color change of the indicator after the addition of the mannitol. The alkali is usually standardized in terms of boric acid by check against samples of known boric acid content.

Biltz and Marcus (4) concluded that with phenolphthatein as the indicator phosphoric acid reacts as a dibasic acid and boric acid in the presence of mannitol as a monobasic acid.

Kolthoff (5) reported the determination of boric acid in the presence of phosphoric acid with phenolphthalein as the indicator. Mannitol was used in the estimation of boric acid. The end point for the titration is at a pH of 8.7.

Vastagh (6) claims no interference results in solutions which have been previously neutralized by potassium hydroxide with methyl red as the indicator when these methods are used except from the presence of silicic acid.

The reliability of the titration methods has been further tested by Foote (7) in his "Determination of Boron in Waters." He concludes that the titration method is the most convenient and reliable of all those studied.

TABLE I

TITRATION RESULTS OF KNOWN AMOUNTS OF BORIC ACID IN URINE
(100 c. c.)

Subject	Amount NaOH Used c. c. N/10	Amount H_3BO_3 Added mg.	Amount H_3BO_3 Found by Titration mg.	Amount H_3BO_3 Found, Per Cent of Total
A	38.78	266.7	239.9	89.9
B	39.43	271.5	243.9	89.8
C	36.98	254.3	228.8	89.8
D	39.50	271.5	244.4	90.0
E	36.15	268.5	223.7	83.3
F	38.00	270.1	235.0	87.0

EXPERIMENTAL

Twenty-four hour samples of urine were collected from six subjects. One hundred cubic centimeter volumes were run from the well-shaken 24 hour collections. No effort was made to control the diet of the subjects—they did not board at the same place—except that each subject ate approximately a uniform diet during the period of the study.

The 100 cc. urine sample was made distinctly acid to methyl red with hydrochloric acid, boiled gently for five minutes, to remove carbon dioxide, cooled and phenol red added. It was then adjusted to a pH of 7.6 by addition of carbon dioxide free sodium hydroxide and approximately 0.1 N hydrochloric acid if necessary. Three grams of mannitol were then added and the titration to a pH of 7.6 repeated. The amount of standard alkali needed for this adjustment in pH is a measure of the quantity of boric acid present. The equivalence of the standard alkali in boric acid was obtained by titration of known strengths of boric acid solutions.

Urine from each of the subjects without the addition of boric acid was titrated as blanks to test the procedure and to determine if it was free from borates. Negative results for borates were obtained in all cases.

Because of the color of the urine samples and the resultant difficulty of determining the end point, it was found necessary to decolorize the urine by means of absorbent charcoal. Tests proved that no measurable loss of boric acid resulted from such decolorization. When these facts were established samples of urine with the addition of known amounts of boric acid were titrated. The results for these tests are given in Table I.

TABLE II

ELIMINATION OF BORIC ACID THROUGH THE URINE

Subject	N/10 NaOH per 100 cc. Urine cc.	Volume Urine Voided cc.	Amount H_3BO_3 Found mg.	Corrected Amount H_3BO_3 mg.	Amount H_3BO_3 Adm. mg.	Amount H_3BO_3 Eliminated First Day. Per Cent of that Administered in Day Determined	Amount H_3BO_3 Eliminated in Two Days. Per Cent of Total Administered
1st day							
A	7.20	1627	724	805	975	82.56	
B	7.97	913	728	810	975	83.08	
C	7.65	760	360	400	975	41.99	
D	6.64	1055	433	481	975	49.33	
E	4.76	1182	348	418	975	42.87	
F	7.09	1477	647	744	975	76.31	
2nd Day						2nd Day	
A	10.25	1150	729	811	975	83.18	82.87
B	8.19	892	452	503	975	51.59	67.33
C	10.76	851	566	630	975	64.65	53.32
D	4.99	1673	516	573	975	58.87	54.10
E	7.98	1093	539	620	975	63.60	53.23
F	6.75	1652	689	792	975	81.23	78.77
3rd Day						3rd Day	Three Days
A	9.31	1715	986	1072	975	109.95	91.89
B	7.29	883	398	442	975	45.41	60.03
C	7.24	1492	668	744	975	76.32	60.65
D	4.55	1620	456	507	975	52.03	53.41
E	4.31	1744	465	527	975	54.06	53.51
F	6.57	1456	957	1100	975	112.82	90.12
4th Day							Four Days
A	3.83	877	208	231	000		100.00
B	3.88	1203	444	495	000		76.92
C	3.72	922	212	236	000		68.72
D	3.35	1090	226	251	000		61.95
E	1.22	1680	127	153	000		59.42
F	2.70	1819	300	349	000		102.05
5th Day							Five Days
A	1.10	1217	83	92	000		102.83
B	0.96	776	46	51	000		78.67
C	1.27	819	64	71	000		71.14
D	0.97	1051	63	70	000		64.34
E	1.10	1100	75	89	000		61.78
F	0.90	1200	66	76	000		104.65

The amount of boric acid actually determined is less than theory. During the course of the experiment, determinations were made on known addition amounts of boric acid to the samples with results that checked the results that are recorded in Table I for the different subjects

under observation. The shortage in amounts determined must be due to the presence of particular buffers or the amounts of buffering materials in the different samples. Phosphates do not appear to be the cause of the difference in behavior as E was low in phosphates, while F was average and other investigators (4) (5) have already stated that phosphates do not interfere with the titration of borates. This individual peculiarity will be investigated further.

Corrections are applied in Table II in all determinations to correct for this divergence from theoretical results.

Blanks were run on a 24 hour sample of each subject before boric acid was administered. Then a total of 975 mg. of boric acid in three equal doses were administered daily at two-hour intervals after the three meals respectively, and 24 hours samples of urine collected (from 7:00 A. M. to 7:00 A. M.). One hundred cubic centimeter samples were taken from the well mixed 24 hour collection and titrated as already described for the blanks. The administration of boric acid was continued for three days and the collection of samples and determination of boric acid for six days, when no boric acid was found.

Tests for boric acid on the sixth and seventh days revealed only traces present that were of no quantitative significance.

The data in Table II indicate that the urinary elimination of boric acid is not uniform but varies with the individual and that one hundred per cent may be eliminated through the urine. This is not in harmony with the reported findings of Wiley (8) who states, that 80 per cent is eliminated through the urine and 3 per cent in the feces and perspiration.

SUMMARY AND CONCLUSIONS

1. Buffers in urine affect the quantitative determination of boric acid and corrections must be applied when the titration method is employed.
2. Quantitative elimination of boric acid through the medium of the urine varies in speed and completeness with the individual.
3. Two of the six cases investigated eliminated 100 per cent of the boric acid administered via the urine.
4. There is a considerable lag in the elimination.

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